

## REMARKS

Claims 1-2, 5-8, 15-20 as amended are pending in the application for the Examiner's reconsideration. All pending claims have been amended to properly italicize the appropriate bacterial strain. Claims 1 and 15 have further been amended to correct some minor informalities and to recite delete reference to gene product, as it is evident to one skilled in the art that a gene product cannot be deleted, but rather the gene encoding it. This amendment is supported by the original claims, for example, original claim 1 and the specification. No new matter has been added, thus entry of the claim amendments is requested. When referring to the specification, Applicants use paragraph numbers as they appear in U.S. Publication No. 2002/0094329.

The Examiner objects to the priority claim, stating that this application should be a continuation of international application PCT/EP99/06818. Applicants agree with the Examiner. Applicants' previous statement that this application was a continuation of the U.S. national stage designation of international application PCT/EP99/06818, filed September 15, 1999, is not contrary to the Examiner's arguments, as the PCT national stage designation is part of the PCT Application. In order to facilitate the allowance of this Application, however, Applicants have amended paragraph [001] to clarify this and request that the objection be withdrawn.

Further, the Examiner objects to the drawing for minor informalities. Applicants submit substitute drawings herewith and respectfully request that the objection be withdrawn.

The Specification, paragraph [001] was also objected to because of certain minor informalities. As stated above paragraph [001] has been amended. Thus, the Examiner's objection has been overcome and should be withdrawn.

Claims 1, 2, 5-8, 15-20 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the reasons set forth on pages 4-5 of the Office Action.

Claims 1 and 15 have been amended so as to delete the phrase "substantial amounts of iso-valeric acids." Applicants appreciate the Examiner's acknowledgement that the phrase "taste perceptible" is not indefinite.

The Examiner further rejected claims 1, 2, 5-8, for indefiniteness stating that the phrase "the *ywfL* gene" was indefinite.

Applicants respectfully traverse. As previously noted, the sequence of the *ywfL* gene is already known in the state of the art. For example, at paragraphs [0015] and [0018],

Applicants point out that the complete genome sequence of the gram-positive bacterium *B. subtilis* can be found in Kunst *et al.*, wherein Kunst *et al.* also discusses the specific gene components of the complete genome. Furthermore, Applicants also provide at paragraphs [0032-0036] that "6626 (SEQ. ID. NO. 2), [is] a composite oligonucleotide comprising 22 bp of the sequence of the region 50 bp away from the start of the *ywfL* gene and 22 bp of the region 100 bp away from the end of the *ywfL* gene." The region between these two sequences is the *ywfL* gene, the region to be deleted or modified. One skilled in the art would know what the *ywfL* gene means, especially in light of Kunst *et al.* and the present teachings by Applicants. Therefore, Applicants respectfully request that the indefiniteness rejection be withdrawn.

Claim 1-6 and 8 were rejected under 35 U.S.C. 112, first paragraph, for lack of written description for the reasons set forth on pages 5-6.

The test for written description is whether one skilled in the art could reasonably conclude that the inventor had possession of the claimed invention. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. [MPEP 2161]. The Examiner argues that "Applicants have not described any of the claimed modifications of the *ywfL* gene product beyond its deletion." Applicants respectfully traverse.

At paragraph [0034] of the specification, Applicants teach that the introduction of two stop codons, TGA, using the oligonucleotide 6626 [SEQ ID NO:2] of the *ywfL* gene, to terminate translation of the *ywfL* gene early. Furthermore, one skilled in the art is aware of other techniques of knocking out gene function, *e.g.*, frame shifting the reading frame by addition or deletion of one or two nucleotides, deletion of start codon, introduction of stop codons, etc. With Applicants disclosure of the invention, one skilled in the art, would reasonably believe that Applicants were in possession of the claimed invention, including a bacterial strain of *B. subtilis* having a *ywfL* gene, which has been deleted or is essentially non-functional. Based on the foregoing, Applicants request that this rejection be with drawn.

Claim 1-6 and 8 were rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for the reasons set forth on pages 7-8. The Examiner states that "while being enabling for *B. subtilis* strain, wherein the *ywfL* gene has been deleted, such that the strain cannot produce substantial amounts of isovaleric acid, does not reasonably provide enablement . . . wherein the *ywfL* gene is essentially non-functional such that the strain cannot produce substantial amounts of isovaleric acid." Applicants traverse.

As explained above, besides the working example of strains wherein the *ywfL* gene has been deleted, Applicants teach in the specification at paragraph [0034] at least one example of how one skilled in the art could provide such a strain, wherein the *ywfL* gene is essentially non-functional. Applicants teach, for example, that two stop codons, TGA, can be introduced using the oligonucleotide 6626 [SEQ ID NO:2] of the *ywfL* gene, which would terminate translation of the *ywfL* gene early. Furthermore, one skilled in the art is aware of other techniques of knocking out gene function, *e.g.*, frame shifting by addition or deletion of one or two nucleotides, deletion of start codon, introduction of stop codons, etc. With Applicants disclosure, and the state of the art at the time of the invention, any experimentation necessary would not be undue. Thus, Applicants respectfully request that the rejection for lack of enablement be withdrawn.

Claims 7 and 19 were rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for the reasons set forth on pages 8-9 of the present Office Action.

Applicants herein provide a "Statement Regarding Microorganism Deposit Under the Terms of the Budapest Treaty," where Applicants agree to make the deposit of strain I-2077 publicly available upon issuance of the patent. In view of this, Applicants request that this rejection be withdrawn.

It is believed that the application is now in condition for allowance, early notification of such would be appreciated. Should the Examiner not agree, a personal or telephonic interview is respectfully requested to discuss any remaining issues and expedite the eventual allowance of the claims. Please feel free to call Allan Fanucci at (212) 294-3311 or Rodney Fuller at (202) 371-5838 if you have any questions to expedite the allowance of all the claims in this application.

Date: \_\_\_\_\_

9-18-03

Respectfully submitted,



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